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10/541,501	07/07/2005	Phaedria Marie St. Hilaire	ST.HILAIRE1A	4075

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,501	ST. HILAIRE ET AL.	
	Examiner	Art Unit	
	TERESA WESSENDORF	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2008 and 07 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43,44,46 and 89-101* is/are pending in the application.

4a) Of the above claim(s) *46,89 and 93-101* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43,44 and 90-92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/23/05 and 5/29/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

The inadvertent exclusion of the newly added claim 90 in the Status of claims in the last Office action and the confusion this might have caused to applicants is regretted. As stated in the last Office action, the then newly added claim 90, being dependent on the elected claim 43, would be examined with the elected claim 43. As correctly pointed out by applicants, claim 90 had been subsequently treated as being rejected under the different statutes (see below), albeit not in the Status of claims.

In response to the species restriction, applicants elected the compound HY6, but requested that the species restriction be withdrawn on the ground that a generic claim is allowable. The Examiner says that this cannot yet be done because "the claimed generic compound has not been found allowable." The only claim rejected over prior art is claim 88 (OA pp. 7-11). Claim 43, which the restriction (page 5, last line) concedes to be generic, was rejected only on written description and indefiniteness grounds, which we believe to have been overcome. In addition, if claim 43 is generic, so too is new claim 91, against which the indefiniteness rejection is clearly irrelevant. In view of the arguments presented below concerning

written description and indefiniteness, claim 43 should be allowed, and the species restriction withdrawn. Applicants state that the examiner has indicated that the isolated ligand HY6 of claim 44 is allowable. Please see the statement below as to the withdrawal of the indicated allowability of claim 44.

Status of Claims

Claims 43-44, 46, 89-101 are pending.

Claims 46, 89 and 93-101 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions and species. (Please note applicants' claim status identifier for claims 46 and 89 as withdrawn). Accordingly, newly added claims 93-103 drawn to the same subject matter as claims 46 and 89 i.e., an isolated ligand-protein binding pair and the method of the alleged use are withdrawn from further consideration. Please see the election/restriction requirement mailed on 6/1/07, withdrawing this subject matter from examination).

Claims 43, 44 and 90-92 are under examination.

Withdrawn Objection/Rejection

In view of the amendments to the claims and applicants' arguments the objection to the specification as given in the last Office action is withdrawn. Also, the 35 USC 112, first

(new matter) and second paragraphs and the 35 US 102/103 over Lohse and Tomlinson rejections are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43 and 90-92, as amended and added, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific identified ligand at pages 128-129, does not reasonably provide enablement for the broad claimed Formula I ligands. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 43 drawn to formula IV ligand(s) is broader in scope than the enabling disclosure. The disclosure enables specific compounds for which specific substituents are defined for the different R variables. See pages 128-129, Table 14. The genus formula IV contains numerous substituents for the three broad R variables (with R3 optionally substituted with any type of substituents). There is no teaching, guidance or direction that

the related species taught in the specification (Example 56 at page 128) is reasonably predictive for the broad scope of Formula IV ligands. The species disclosed in the specification do not teach or describe a single species that contain any of the numerous claimed amino acids, natural or unnatural, singly or in combinations included in Formula IV. Further, there is no enabling disclosure as to the kind and/or number of optional substituents that is encompassed by the R3 variable. Formula IV includes a huge, infinite library of compounds for which no known use has been identified for either each of the ligand (member) or for the single entire genus compound (library). The specification provides only a listing of e.g., the amino acids, as claimed. However, a listing or definition of every possible amino acids or optional substituents(for R3) does not constitute a written description of every species in a genus. It would not "reasonably lead" those skilled in the art to any particular species. In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967).

The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include:

(1) the breadth of the claims,

(2) the nature of the invention,
(3) the state of the prior art,
(4) the level of one of ordinary skill;
(5) the level of predictability in the art,
(6) the amount of direction provided by the inventor,
(7) the existence of working examples, and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.
In re Wands, (U.S.P.Q. 2d 1400 (CAFC 1988).

1). The specification fails to give adequate direction and guidance in how to readily go about determining the kind/type, singly or in combination the amino acids included or precluded in Formula 4 and the kind, location and length of the optional substituents for R3 variable. The disclosure fails to teach the experimental conditions, reagents and other experimental factors in the making of the other species of Formula IV, which contains different structural base. That is, whether the experimental conditions use for diazepine like molecule (page 128) are similarly applicable to the structurally different compound containing amino acids or optional substituents of Formula IV.

2). The specification failed to provide working examples for any of the numerous and different type of compound-containing amino acids or optional substituents, singly or in combination.

3). The breadth of the claims encompasses a large diversity of the base ligand (Formula IV) for with the related species diazepine would not suffice as enabling disclosure. It

is well known in the art, that it is often difficult to know what amino acid insertions in Formula IV can be made without deleteriously affecting the ligand function or its global structure. The diversity of the inserts is not easily estimated. There remain distinct deficiencies in the methods used to isolate and identify ligands to be considered functional.

4). The state of the prior art is such that special and specific techniques are specifically applied for a specific base ligand and mutations thereof.

5). The art is inherently unpredictable because it is not possible to predict which predetermined (variations) of amino acids would result in the desired ligand with a desired function. Some amino acids can be accommodated at different sites (R1 and R2) in Formula IV. Others are much less accommodating. It is difficult in general to predict whether Formula IV is robust to variations of amino acids, natural or non-natural, and which sites (R1-R3) are best suited to variations of multiple independent residues (or sequences). The complex spatial configuration of amino acid side chains and the interrelationship of different side chains in these sites are insufficiently understood to allow for such predictions.

6). Because the art is unpredictable, applicants' specification reasonably would not have assured persons skilled in the art that the numerous undefined molecule in Formula IV would result in a mutations having function without undue experimentation. Applicants do not adequately enable persons skilled in the art to readily determine such. Applicants need not guarantee the success of the full scope of the claimed invention. However, skilled artisans are provided with little assurance of success or guidance.
[This rejection can be overcome by claim 44 or the species recited at pages 128-129 of the instant disclosure).

Claim Rejections - 35 USC § 112, second paragraph

Claims 43 and 90-92, as amended and newly added, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 90 is indefinite in the recitation of the "group consisting of compound 3 **to** 47". However, there are no e.g., compounds 5-11 as set forth in the recited structures. [It is suggested that the compounds set forth be given the acronyms e.g., Ala, Gly, Phe, Ile and so on without the structures. The

structures of these amino acid residues are known in the art. Thus, the acronyms would suffice, except, of course for the non-amino acids e.g., structures 117-126. As applicants stated in the REMARKS errors made in the structures can lead to a new matter issue]. This rejection has similar import to claim 92.

2. Claim 91 is a duplicate of claim 43. Applicants state that claim 43 explicitly claims what the dotted lines stand for. Accordingly, claim 43 lacks antecedent basis of support from the specification. As stated by applicants, claim 91 finds support in the specification at page 39, lines 15-30. {It is suggested that claim 91 be claimed in lieu of claim 43].

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or

provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 43 and 90-92, as amended and newly added, are provisionally rejected on the ground of nonstatutory double patenting over the copending Application No. 10/346,737. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is **fully disclosed** in the referenced copending application, S.N. 10/346,737 and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows: the claimed Formula IV is identical and fully disclosed at e.g., page 68, Example 36 of the copending application S.N. 10/346,737.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

The indicated allowability of claim 44 in the last Office action is withdrawn in view of the newly discovered reference(s) below. Rejections based on the newly cited reference(s) follow.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 43 and 90-92, as amended and newly added, are rejected under 35 U.S.C. 102(b) as anticipated by St. Hilaire et al (Journal of the American Chemical Society (1998), 120(51), 13312-13320).

St. Hilaire et al discloses throughout the article at e.g., page 13312, abstract:

The most active glycopeptides detected from the library screening were T(α-D-Man)ALKPTI-IV, LHGGFT(α-D-Man)HV, T(α -D-Man)EHKGSKV, GT(α -D-Man)FPGLAV, and T(α -D- Man) LFKGFI-IV.

Accordingly, the species recited by St. Hilaire is included in the broad claimed Formula IV and anticipates the broad claimed Formula IV.

Claims 43 and 90-92, as amended and newly added, are rejected under 35 U.S.C. 102(b) as anticipated by Shaw et al(USP 5696260) or applicants' disclosure of known prior art.

Shaw discloses throughout the patent at e.g., col. 5, line 5 up to col.12, line 55 a compound structure of the given formula I. Accordingly, the specific compound of Shaw fully meets the broad claimed formula IV.

Applicants disclose at e.g., page 129, compound 3 i.e., HY6 as Myosin chain (Q63358); NF-kappa B-repressing factor (Transcription factor ITBA4 protein) (015226). These compounds are known. (See e.g., Shaw above).

Applicants further disclose at e.g., page 107, lines 13-25:

> Library 5…….was designed to create diazepine-like templates (when n = 3) and isoindolone-type compounds. Many benzodiazepines have potent biological activities (see Pigeon et al, 1998, Tetrahedron, 54: 1497-1506). Isoindolone-type compounds possess anti-inflammatory, analgesic, blood pressure lowering, spasmolytic….properties.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the

art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 43-44 and 90-92, as amended and added, are rejected under 35 U.S.C. 103(a) as being unpatentable over Shaw et al.

Shaw is discussed above. The compound of Shaw includes or encompasses the claimed HY6. See the above-cited sections.

Applicants' arguments with respect to Lohse and Tomlinson are moot in view of the new rejection above.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is(571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on (571) 272-0765. The fax phone number for the organization where this application or proceeding is assigned is 571 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/TERESA WESSENDORF/

Primary Examiner, Art Unit 1639